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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,424	07/11/2003	Alexis Borisy	50164/022002	3223

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EXAMINER	
WEDDINGTON, KEVIN E	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/617,424	BORISY ET AL.	
	Examiner	Art Unit	
	Kevin E. Weddington	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *30-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29 and 36-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-39 are presented for examination.

Applicants' information disclosure statement filed June 9, 2004 has been received and entered.

Applicants' election filed September 20, 2004 in response to the restriction requirement of August 17, 2004 has been received and entered. The applicants elected the invention described in claims 1-29 (Group I) without traverse. Claims 36-39 will be examined with the elected invention.

Claims 30-35 are withdrawn from consideration as being drawn to the non-elected invention. (37 CFR 1.142(b))

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11, 19-29 and 39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 and 35 of U.S. Patent No. 6,569,853. Although the conflicting claims are not identical, they are not patentably

distinct from each other because the claims of the present application are generic to all that is recited in the claims of U.S. Patent 6,569,853. That is, the claims of U.S. Patent 6,569,853 fall entirely within the scope of the claims of the present application, or in other words, claims 1-11, 17, 19-29 and 39 are anticipated by claims 1-24 and 35 of U.S. Patent 6,569,853. Specifically, U.S. Patent 6,569,853 claims combination compositions containing chloropromazine and pentamidine compounds and methods of using said compositions for treating neoplasms (leukemia, liver, colon, prostate, lung cancer, etc.), wherein the chloropromazine and pentamidine compounds fall within claimed formulae (I) and (II).

Claims 1-11, 19-29 and 39 are not allowed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 and 17-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,846,816. Although the conflicting claims are not identical, they are not patentably distinct from each other

because the claims of the present application are generic to all that is recited in claims of U.S. Patent 6,846,816. That is, the claims of U.S. Patent 6,846,816 fall entirely within the scope of the claims of the present application, or in other words, claims 1-11 and 17-29 are anticipated by claims 1-13 of U.S. Patent 6,846,816. Specifically, U.S. Patent 6,846,816 claims combination compositions containing chloropromazine and pentamidine compounds and methods of using said compositions for treating neoplasms (leukemia, liver colon, prostate, lung cancer, etc.), wherein the chloropromazine and pentamidine compounds fall within claimed formulae (I) and (II). Note the addition of other antiproliferative agents or chemotherapeutic agents as disclosed in claims 17 and 18 of the present application and claim 5 of U.S. Patent 6,846,816.

Claims 1-11 and 17-29 are not allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-29 and 36-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for chloropromazine of formula (I) and pentamidine of formula (II) to treat lung cancer, does not reasonably provide enablement for other compounds derived from formulae (I) and (II) of claim 1 or the addition of a third agent as disclosed in claims 17 and 18 with the combination of chloropromazine and pentamidine to treat all types of neoplasms. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make/and use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation.

The factors include:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provided guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to compositions and methods for treating a patient having a neoplasm comprising administering to said patient a composition comprising a first compound

derived from formula (I) and a second compound derived from formula (II) simultaneously or within 14 days of each other, in amounts sufficient to inhibit the growth of said neoplasm. Note the addition of a third compound (an antiproliferative agent) can be combined with the instant composition.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

The present invention is unpredictable unless experimentation is shown for the other compositions comprising other compounds of formula (I) and other compounds of formula (II), additional combined with a third agent (antiproliferative agent) to treat types of neoplasms.

The breadth of the claims

The claims are very broad and inclusive to all compositions comprising the combination of all compounds of formula (I) and all compounds of formula (II).

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the administration of a composition comprising chloropromazine derived from formula (I) and pentamidine derived from formula (II) in human lung adeneocarcinoma tumor cell line and human lung tumor graft.

No working examples showing for the addition of the third agent. No working examples showing the instant composition to treat other types of neoplasms or there no working examples showing the other compounds derived from formula (I) and formula (II) combined into a single composition to treat all types of neoplasms.

The quantity of experimentation necessary

Applicants have failed to provided guidance to how the other compounds of formula (I) and the other compounds of formula (II) combined into a single composition, used alone or with combined with a third agent is effective in treating neoplasms. The level of experimentation needed to determine the other compounds derived from formulae (I) and (II) would be able to treat neoplasms is undue. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 1-29 and 36-39 are not allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is rendered indefinite and vague by the phrase "an additional treatment of cancer". The applicants have not disclosed what is the "additional treatment of cancer" administer in conjunction with a composition containing compounds derived from formulae (I) and (II). Claims 13-16 are rendered indefinite to the extent that they incorporate the above terminology.

Claims 12-16 are not allowed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 17-29 and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dwivedi et al., "Effects of Treatment with Haloperidol, Chloropromazine, and Clozapine on Protein Kinase C (PKC) and Phoshoinositide-Specific Phospholipase C (PI-PLC) Activity and on mRNA and Protein Expression of PKC and PLC Isozymes in Rat Brain", The Journal of Pharmacology and Experimental Therapeutica, 1999, Vol. 291, pp. 688-704 in view of Makulu et al. (PTO-1449) and further in view of Windholz et al., THE MERCK INDEX,(1983), Tenth Edition, page 183, abstract no. 1308.

Dwivedi et al., teach chloropromazine has been investigated for the inhibition of protein kinase C in vivo studies (See the abstract). One skilled in the art knows the activity of protein kinase C mediates the effects of a large number of hormones and is involved in many aspects of cellular regulation and carcinogensis. And the enzyme is also thought to play a role in certain types of resistance to cancer chemotherapeutic agents. Since Dwivedi et al., teach chloropromazine inhibits the activity of protein kinase C (known to resist chemotherapeutic agents) then one skilled would have assumed chloropromazine possesses anti-neoplasm activity as suggested in applicants' specification on page 31, lines 18-25.

The instant invention differs from the cited reference in that the cited reference does not teach the addition of a second compound derived from formula (II) combined with chloropromazine, a compound derived from formula (I) to treat neoplasm. However, the secondary reference, Makulu et al., teaches pentamidine (a compound derived from formula (II) possesses anti-tumor properties. (see the abstract) Clearly, one skilled in the art would have assumed the combination of two individual compounds, both known to possess anti-neoplasm and anti-tumor activities into a single composition to treat neoplasm would give an additive effect in the absence of evidence to the contrary.

Concerning the timing of administering of the two compounds (claims 1-10), it would have been obvious to one skilled in the art at the time the invention was made to further modify the method of Dwivedi et al and Makulu et al. to administering the compounds as such a time as to optimize each compound's efficacy against the cancer being treated.

The instant invention differs from the cited references in that the cited references do not teach the addition of a third agent, an antiproliferative agent (claims 17 and 18) combined with the instant composition to treat neoplasms. However, the tertiary reference, Windholz et al., teaches one of the applicants' preferred antiproliferative agent, bleomycin, is well-known to treat neoplasms. Clearly, one skilled in the art would have assumed the addition of the third agent to the instant composition of the present application, known to possess anti-neoplasm activity, into a single composition to treat neoplasm would give an additive effect in the absence of evidence to the contrary.

Finally, modification of the compositions by packing them in a container resulting in a kit (claims 36-38) would have been obvious to one skilled in the art since pharmaceutical compositions are routinely employed into pharmaceutical packs or kits from distribution of the product to the general public.

Claims 1-11, 17-29 and 36-39 are not allowed.

The remaining references listed on the enclosed PTO-892 are cited to show the state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 11:00 am-7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0953. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kevin E. Weddington
Primary Examiner
Art Unit 1614

K. Weddington
February 7, 2005